REMARKS/ARGUMENTS

Claims 4 and 11 are now pending. Applicants hereby cancel claims 9-10. Applicants also amend claim 4 to define what is meant by an inhibitor of Vav protein. Support can be found in the application as filed on pages 2-5. Applicants further add new claim 11, which recites that the inhibitor of a Vav protein of claim 4 is a Vav1 binding antibody. Support for this amendment is found in the specification, paragraph bridging pages 2-3. No new matter has been added.

Claim objections

The Examiner has objected to informalities in claims 9 and 10. Applicant has cancelled these claims. Accordingly, this objection is now moot.

Rejections under §112, second paragraph, indefiniteness

The Examiner has rejected claim 4 for alleged indefiniteness. Applicants have amended claim 4 as suggested by the Examiner to recite the phrase "selected from the group consisting of". Applicants also have replaced the term "therapeutic combination" with the more common term "pharmaceutical composition". Support may be found in the specification at page 15, point 1.9. No new matter is added.

Accordingly, the pending claims are now definite. Applicants respectfully request that this rejection be withdrawn.

Rejections under §112, first paragraph, written description

The Examiner has rejected claims 4 and 9-10 for alleged lack of written description. Applicants have amended claim 4 to define what is mean by an inhibitor of Vav protein. In particular, the claim now recites an inhibitor of Vav1 protein. Support for this amendment can be found in the specification at least at pages 2-5. Vav1 protein is well known in the art as a GEF factor, as explained in the introduction at page 1 of the patent specification. The patent specification also provides sufficient description how to obtain inhibitors of Vav1 protein without undue burden. Examples of such Vav1 inhibitors can be anti-Vav1 antibodies.

In addition, Applicants have canceled claims 9-10. Accordingly, the pending claims are now adequately described in the specification. Applicants respectfully request that this rejection be withdrawn.

Rejections under §112, first paragraph, enablement

The Examiner has rejected claim 10 for alleged lack of enablement. Applicants have canceled claim 10. Accordingly, this rejection is now moot.

Rejection under §102

The Examiner has rejected claim 9 for alleged lack of novelty over Piccolella *et al.*, *J. Immunology* 170:2895-2903 (2003) ("*Piccolella*"). Applicants have canceled claim 9. Accordingly, this rejection is now moot.

Rejections under §103, obviousness

The Examiner has rejected claims 4 and 9-10 as allegedly unpatentable in view of U.S. Pat. No. 6,323,317 to Hilton *et al.* ("*Hilton*") in view of Sepulveda *et al.*, J. Biol. Chem. 275:14005-14008 (2000) ("*Sepulveda*"). The Examiner alleges that it would have been obvious to have substituted SOCS-1 as a Vav-1 inhibitor in a pharmaceutical composition as taught by *Hilton* for an anti-Vav-1 antibody as taught by *Sepulveda*. Applicants respectfully traverse.

The present invention provides for the first time clear *in vivo* indication that inhibition of Vav1 protein activity increase graft survival in a mammal (here a mouse) and therefore could be used in the treatment of prevention of graft rejection, and more generally inflammatory or autoimmune diseases or T-cell leukemias or lymphomas (see *e.g.* specification page 16, Table 1). Absent any *in vivo* data (such as those provided in the present invention), there would be no motivation for the one skilled in the art to use Vav1 inhibitor in combination with immunosuppressant, immunomodulatory or anti-inflammatory drugs as claimed in new claim 4.

The advantages provided by the combination of active agents of the present invention are very different from the combination taught by *Hilton* in the passage cited by the Examiner (*Hilton*, "column 30, second full paragraph, in particular, line 30"). The second agents taught by Hilton are "various antibacterial and antifungal agents" for the "preventions of the action of microorganisms" on the "sterile injectable solutions" which "must be preserved against the contaminating action of microorganisms such as bacteria and fungi".

Hilton recite SOCS genes, and in particular SOCS1 gene. However, there is no teaching or suggestion that SOCS genes and the protein encoded by this gene could have a role in inflammatory responses or preventing or treating graft rejection. Therefore, the one skilled in the art would find no motivation from *Hilton* combine it with immunosuppressant, immunomodulatory or anti-inflammatory drug. *Sepulveda* merely report evidence suggesting a role of SOCS1 in the destruction of VAV protein. No further indication regarding potential use of SOCS1 in combination immunosuppressant, immunomodulatory or anti-inflammatory drug could be derived from *Sepulveda*.

Accordingly, the pharmaceutical composition of claim 4 is not obvious in view of a combination of *Hilton* and *Sepulveda*. Applicants respectfully request that this rejection be withdrawn.

An early and favorable action on the merits is respectfully requested. Should the Examiner have any questions, please contact the undersigned attorney.

Respectfully submitted,

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